REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Objection to the Specification

The specification is objected to for having an allegedly non-descriptive title. The specification has been amended to replace the title of the invention with a new title, which is essentially in line with the Examiner's suggestion.

It is acknowledged that this amendment is made after final rejection. However, because the amendment does not introduce new matter, and either places the application in condition for allowance or at lease in better condition for appeal, entry thereof by the Examiner is respectfully requested.

II. Statement of the Substance of the Examiner's Interview

Applicants thank Examiner James Alstrum-Acevedo for the courtesies extended during an interview with Applicants' representative, Yang Tang, on July 6, 2011. During the interview, the patentability of claims 28, 73 and 74 was discussed. Examiner Alstrum-Acevedo indicated that claim 74 was not rejected over the cited art, but was subject to additional search.

III. Rejection of Claims under 35 U.S.C. §103(a)

A. Liversidge, Pavord, Glaxo History, Merck Index, Radhakrishnan and Palmer

Claims 28-36, 39-40, 51-60 and 64-73 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over U.S. Patent No. 5,145,684 to Liversidge et al. ("Liversidge") in view of Pavord et al., *Clin. Pharmacokinet.*, 25(2) (1993), abstract ("Pavord"), Glaxo History (www.gsk.com/about/history-noflash.htm), and the Merck Index, 10th ed., page 144, entry 1018

("Merck Index"), as evidenced by U.S. Patent No. 5,049,389 to Radhakrishnan et al. ("Radhakrishnan") and U.S. Patent No. 5,208,226 to Palmer et al. ("Palmer"). Applicants respectfully traverse the rejection.

(1) The Examiner erroneously dismissed the declaration evidence.

The Examiner dismissed the Bosch Declaration submitted in the prior response on the grounds that: (i) the comparison of the claimed invention with Vanceril® is "an apples and oranges comparison" because two different devices are used for the claimed composition; and (ii) Applicants fail to compare the claimed invention with the closest prior art, Liversidge. *See* final Office Action, page 4.

First, the declaration explains that an ultrasonic nebulizer was *not an option* for aerosol delivery of *conventional, non-nanoparticulate* water-insoluble drugs, such as beclomethasone, due to inefficient aerosolization. To demonstrate this fact, delivery of Vanceril® , which comprises conventional, non-nanoparticulate beclomethasone (e.g., a poorly water soluble drug) in a propellant-based device, was evaluated. *See* Bosch Declaration, paragraphs 10 and 11. The results of this experiment confirmed that an ultrasonic nebulizer "was not feasible for delivering water-insoluble [conventional, non-nanoparticulate] active agents due to a lack of efficient aerosolization." *See* Bosch Declaration at paragraph 10.

Applicants' claimed invention *solved* this problem present in the prior art. Specifically, the claimed invention enables the efficient delivery via an ultrasonic nebulizer of the nanoparticulate poorly water-soluble active agent beclomethasone due to the small particle size of the beclomethasone. This result achieved by the claimed invention is unexpected as compared to a commercial, non-nanoparticulate beclomethasone formulation. *See* Bosch Declaration at paragraph 11, reproduced below:

11. The claimed nanoparticulate beclomethasone dipropionate composition was capable of being delivered by an ultrasonic nebulizer. Unexpectedly, superior delivery efficiency of the claimed nanoparticulate beclomethasone dipropionate composition was achieved in comparison to the commercial formulation, Vanceril®, delivered by a propellant-based MDI, as detailed below.

Applicants' comparison of the nanoparticulate beclomethasone dosage form of the claimed invention to a prior art conventional, non-nanoparticulate beclomethasone dosage form was proper per the M.P.E.P. Specifically, pursuant to MPEP 716.02(e), "Applicants may compare the claimed invention with prior art that is more closely related to the invention than the prior art relied upon by the examiner. *In re Holladay*, 584 F.2d 384, 199 USPQ 516 (CCPA 1978); *Ex parte Humber*, 217 USPQ 265 (Bd. App. 1961)."

Second, the Examiner has failed to establish that Liversidge is the closest art. MPEP 716.02(e) has the following guidance in terms of the "closest art":

> *. . . applicant is not required to compare the claimed invention with subject matter that does not exist in the prior art. . . . In re Chapman, 357 F.2d 418, 148 USPQ 711 (CCPA 1966) (Requiring applicant to compare claimed invention with polymer suggested by the combination of references relied upon in the rejection of the claimed invention under 35 U.S.C. 103 "would be requiring comparison of the results of the invention with the results of the invention." 357 F.2d at 422, 148 USPQ at 714.).*

In the present case, Liversidge neither discloses the active agent of the claimed invention (beclomethasone) nor discloses an aerosol formulation. Therefore, it is unclear why Liversidge is the closest prior art to the claimed invention.

Third, the Bosch Declaration established that a nanoparticulate beclomethasone formulation of the claimed invention unexpectedly achieved higher nebulization efficiency in comparison to prior art conventional, microparticulate beclomethasone formulations (*e.g.*,

Vanceril®). The Examiner does not deny the unexpected high nebulization efficiency but fails to articulate why the unexpected results do not rebut the rejection.

For at least these reasons stated above, the pending claims are nonobvious over the combination of the cited references.

(2) Claim 74 benefits from additional grounds of patentability.

During the Examiner's interview, the Examiner confirmed that claim 74 is nonobvious over the cited references on the record. Should the Examiner find claim 74 allowable, Applicants respectfully request that the recitations of claim 74 be incorporated in the base claims by way of an Examiner's Amendment or by an Applicants' supplemental amendment.

B. Liversidge, Pavord, Glaxo History, Merck Index, Radhakrishnan, Palmer and Spear

Claims 42-43 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Liversidge in view of Pavord, Glaxo History, and the Merck Index, as evidenced by Radhakrishnan and Palmer, and further in view of U.S. Patent No. 5,525,623 to Spear et al. ("Spear"). Applicants respectfully traverse the rejection.

The Examiner asserts that Spear compensates for the deficiencies of the other cited references by teaching a jet nebulizer or an ultrasonic nebulizer. *See* final Office Action, page 14, 3rd paragraph. The Examiner's interpretation of Spear is taken out of context because Spear *fails to teach using a jet nebulizer or an ultrasonic nebulizer for a poorly-soluble active agent or a composition in which the active agent existed in a particulate form.* Rather, Spear teaches the use of a jet nebulizer or an ultrasonic nebulizer for a *solution.* The relevant content of Spear is excerpted below:

> *In one embodiment, devices of the present invention comprise* ***solutions of the compounds*** *of the instant invention connected to or contained within any of the conventional means* ***for creating aerosols*** *in asthma medication, such as*

metered dose inhalers, jet nebulizers, or ultrasonic nebulizers. Optionally such device may include a mouthpiece fitted around the orifice.

Spear, column 13, lines 34-40. Accordingly, the skilled artisan would not have any reason to combine the teaching of Spear, which relates to aerosolization of a *solution* rather than a particulate active agent composition, particularly in view of the Bosch Declaration teaching the failure of such devices to successfully deliver prior art particulate dosage forms (*see e.g.*, paragraphs 10 and 11 of the Bosch Declaration).

In view of the foregoing, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103(a).

IV. Provisional Double Patenting Rejection

Claims 28-33, 39-40, 51-60, 66, 69 and 72 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-7, 9-11, and 13-14 of copending Application No. 10/035,324 entitled "Sterile Filtered Nanoparticulate Formulations Of Budesonide And Beclomethasone Having Tyloxapol As A Surface Stabilizer" ("the '324 application") in view of Liversidge and Radhakrishnan.

Claims 28-33, 53-60, 66, 69 and 72 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 60-61, 64-65, 69-70 and 72-76 of copending Application No. 10/768,194 entitled "Novel Fluticasone Formulations" ("the '194 application") in view of Liversidge and Radhakrishnan.

Finally, claims 28-36 and 51-60 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-11 and 17-18 of copending Application No. 12/292,092 entitled "Nanoparticulate Compositions Of Immunosuppressive Agents" ("the '092 application") in view of Liversidge and Radhakrishnan. Applicants respectfully traverse each rejection.

The '194 application has been abandoned, thereby rendering the rejection moot. Applicants choose to defer any action for the provisional double patenting rejection over the '324 and the '092 applications until the Examiner indicates that the pending claims are otherwise allowable.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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